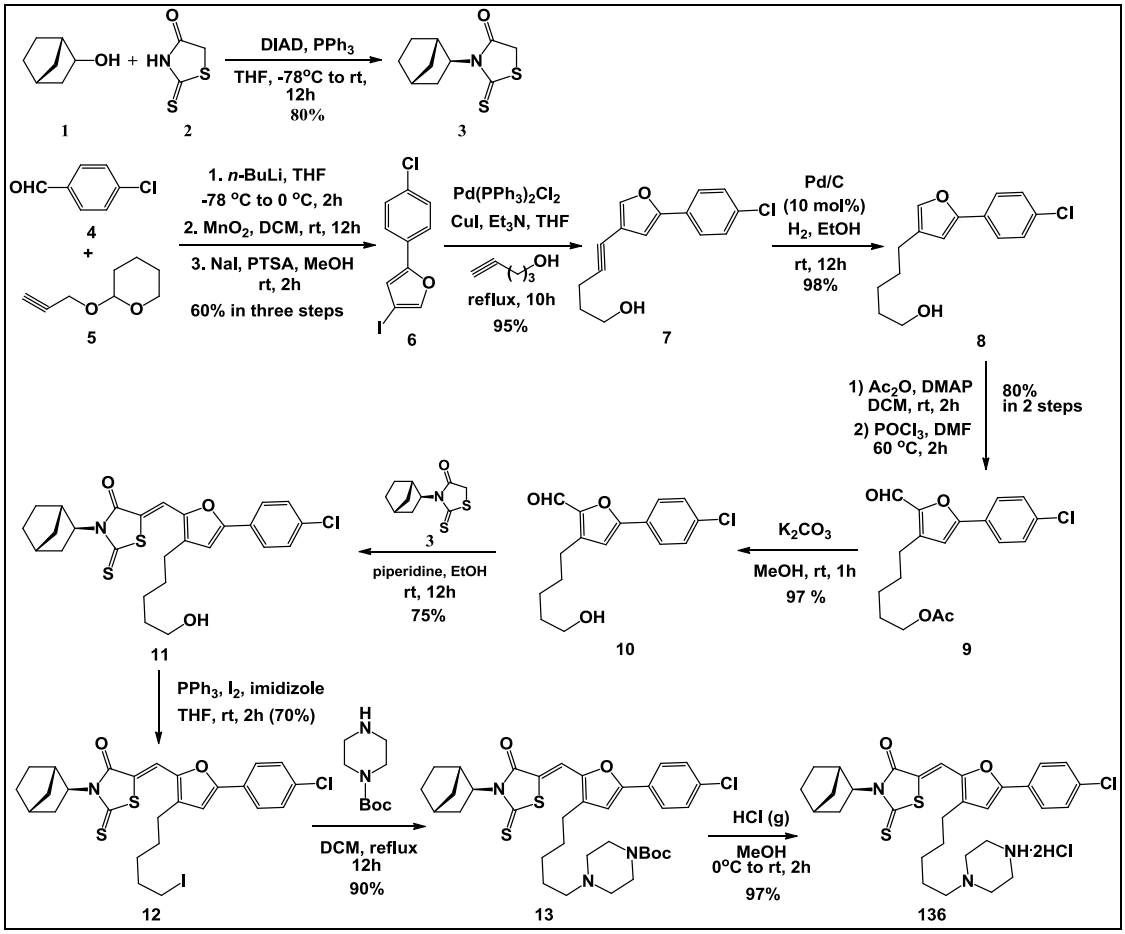
S1 File. Synthesis of compounds 136 and 211.

Anhydrous THF and dioxane were distilled from sodium-benzophenone, and dichloromethane was distilled from calcium hydride. All starting materials were purchased from either J&K Chemicals Co. or Sigma Aldrich Chemical Co.. P25H2 was purchased from ChemDiv, Inc. Water was distilled and purified through a Milli-Q water system (Millipore Corp., Bedford, MA). All reactions were carried out under a nitrogen atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm Tsingdao silica gel plates (60F-254) using UV light as visualizing agent and an ethanolic solution of phosphomolybdic acid and potassium permanganate, and heat as developing agents. Tsingdao silica gel (60, particle size 0.040–0.063 mm) was used for flash column chromatography to purified compounds. Yields refer to chromatographically, unless otherwise stated. All compounds were characterized by ^{1}H and ^{13}C-NMR using Bruker 300 MHz NMR and/or Bruker 400 MHz NMR spectrometers. Chemical shifts are reported in ppm (δ) relative to the residual solvent peak in the corresponding spectra; chloroform δ 7.26 and δ 75.5, DMSO-d_6 δ 2.54 and δ 39.5, and coupling constants (*J*) are reported in hertz (Hz) (where, s = singlet, b = broad, d = doublet, dd = double doublet, bd = broad doublet, ddd = double doublet of dublet, t = triplet, td = double triplet, q = quartet, m = multiplet). Mass spectra values are reported as *m/z*.
Abbreviations: NaH = sodium hydride, PPh_3 = trilphenylphosphine, DIAD = diisopropyl diazene-1,2-dicarboxylate, THF = tetrahydrofuran, DCM = dichloromethane, EA = ethyl acetate, DMF = dimethylformamide.

- General procedure for the synthesis of *(Z)*-(+/-)-*exo*-3-(bicyclo[2.2.1]heptan-2-yl)-5-((5-(4-chlorophenyl)-3-(5-(piperazin-1-yl)-pentyl)furan-2-yl)methylene)-2-thioxothiazolidin-4-one dihydrochloride **136**:



Synthetic route of inhibitor **136**

Synthesis of (+/-)-*exo*-3-(bicyclo[2.2.1]heptan-2-yl)-2-thioxothiazolidin-4-one **3**:

To a solution of triphenylphosphine (6.3 g, 24 mmol) in THF (150 mL) was added DIAD (5.2 g, 24 mmol) at -78 ºC within 2 minutes, and the resultant mixture was stirred at the same temperature for 10 minutes followed by the addition of 1-bicyclo[2.2.1]-heptan-2-ol (mixture of *endo* and *exo*, purchased from Sigma Aldrich Chemical Co., 3.4 g, 30 mmol) at the same temperature. After stirring for 10 minutes rhodanine (2.7 g, 20 mmol) was added to the above solution at -78 ºC, and the resultant mixture was first stirred at -78 ºC for 10 minutes, and then warmed to room temperature, and stirred for 12 h. The reaction was worked up by addition of water (30 mL), and the formed solid was filtered off, and the aqueous phase was extracted with ethyl acetate (3 x 30 mL). The combined organic extracts were washed with brine (20 mL), and dried over anhydrous Na_2SO_4. After removal of the solvent under vacuum, the residuce was purified by a flash column chromatography on silica gel (ethyl acetate-hexane) to give (+/-)-*exo*-3-(bicyclo[2.2.1]heptan-2-yl)-2-thioxo- thiazolidin-4-one **3** (3.6 g) in 80% yield as pale yellow solids; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.78 (td, J = 8.4, 6.3 Hz, 1H), 3.84 (s, 1H), 2.46 (s, 1H), 2.42 (s, 1H), 2.25-2.13 (m, 2H), 1.76-1.56 (m, 4H), 1.40-1.10 (m, 2H); HRMS (ESI) calcd for $C_{10}H_{14}NOS_2$ $[M + H]^+$ 228.0517, found 228.0510.

Synthesis of 2-(4-chlorophenyl)-4-iodofuran **6**:

To a stirred solution of THP-protected propargylic alcohol **4** (16.8 g, 0.12 mol) in dry THF (100 mL) was added *n*-BuLi (0.12 mol, 2.5 M in hexane) at -78ºC, and the mixture was stirred for 30 min at -30 ºC, followed by addition of the aldehyde **5** (14.0 g, 0.10 mol) in THF

(50 mL) at -78 ºC. The mixture was stirred for 30 min at -78ºC, followed by reaction at 0 ºC for 30 min at 0 ºC.The reaction was worked up by addition of a saturated ice/water solution of NH_4Cl (100 mL), followed by Et_2O (100 mL) and the mixture was extracted with ethyl acetate (3 x 50 mL). The combined organic extracts were washed with saturated brine, and then dried with $MgSO_4$. The solvent was removed under vacuum, and the residue was dissolved in DCM (50 mL). To this solution was added to a solution of a solution of active MnO_2 (3.0 mol) in DCM (100 mL) at room temperature, and the mixture was stirred for 12 h. The reaction was worked up by filtration, and the filtrate was dried with $MgSO_4$.

The solvent was removed under vacuum, and the residue was redissolved in methanol (100 mL). To this solution was added sodium iodide (75.0 g, 0.50 mol), *p*-toluenesulfonic acid monohydrate (19.0 g, 0.10 mol) at room temperature, and the reaction mixture was stirred at the same temperature for 2 h. The reaction mixture was worked up by addition of a saturated solution of $NaHCO_3$ and Na_2SO_3, and the resultant mixture was extracted with CH_2C1_2. The combined organic extracts were dried with $MgSO_4$.The solvent was concentrated under vacuum,and the residue was purified by a flash chromatography on neutral aluminium oxide (hexane/ethyl acetate) to give 4-iodo-2-(4-chlorophenyl)-4-iodofuran **6** (18.2 g, 60%) as pale yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 (d, J = 13 Hz, 2H), 7.46 (s, 1H), 7.35 (d, J = 11 Hz, 2H), 6.71 (s, 1H); HRMS (ESI) calcd for $C_{10}H_7ClIO$ $[M + H]^+$ 304.9230, found 304.9228.

Synthesis of 5-(5-(4-chlorophenyl)furan-3-yl)pent-4-yn-1-ol **7**:

To a solution of 2-(4-chlorophenyl)-4-iodofuran **6** (3.04 g, 10.0 mmol) and pent-4-yn-1-ol (1.68 g, 20.0 mmol) in degassed THF (80 mL) was sequentially added $Pd(PPh_3)Cl_2$ (0.70 g, 1.0 mmol), CuI (0.38 g, 2.0 mmol) and Et_3N (5.05g, 50.0 mmol), andthe reaction mixture was stirred for 10 h under refluxing conditions. The reaction was worked up by removal of the solvent under vacuum, and the residue was purified by a flash chromatography (hexane/ethyl acetate) on silica gel to give 5-(5-(4-chlorophenyl)-furan-3-yl)pent-4-yn-1-ol **7** (2.47 g, 95%) as yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55 (d, J = 6.5 Hz, 2H), 7.33 (d, J = 6.5 Hz, 2H), 7.26 (s, 1H), 6.53 (d, J = 1.8 Hz, 1H), 3.72 –3.69 (m, 2H), 2.56 –2.53 (m, 2H), 1.89-1.82 (m, 2H), 1.67 (board, 1H); HRMS (ESI) calcd for $C_{15}H_{14}ClO_2$ $[M + H]^+$ 261.0682, found 261.0680.

Synthesis of 5-(5-(4-chlorophenyl)furan-3-yl)pentan-1-ol **8**:

To a solution of 5-(5-(4-chlorophenyl)furan-3-yl)pent-4-yn-1-ol **7** (2.00 g, 7.7 mmol) in EtOH (50 mL) was added 10% Pd/C (0.20 g), and the mixture was stirred under a balloon pressure of hydrogen for 12 h.. The reaction was worked up by filtration of the reaction mixture, and the filtrate was concentrated, and the residue was purified by a flash chromatography (hexane/ethyl acetate) on silica gel to give 5-(5-(4-chlorophenyl)furan-3-yl)pentan-1-ol **8** (2.03 g, ~100%) as the pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55 (d, J = 8.7 Hz, 2H), 7.33 (d, J = 8.7 Hz, 2H), 7.23 (d, J = 0.9 Hz, 1H), 6.53 (s, 1H), 3.66 (t, J = 6.0 Hz, 2H), 2.45 (t, J =7.5 Hz, 2H), 1.65-1.56 (m, 6H), 1.49-1.40 (m, 2H); HRMS (ESI) calcd for $C_{15}H_{18}ClO_2$ $[M + H]^+$ 265.0995, found 265.0999.

Synthesis of 5-(5-(4-chlorophenyl)-2-formylfuran-3-yl)pentyl acetate **9**:

To a solution of 5-(5-(4-chlorophenyl)furan-3-yl)pentan-1-ol **8** (2.03 g, 7.7 mmol) in DCM (50 mL) was added Ac_2O (3.11 g, 30.8 mmol) and DMAP (0.10 g, 0.8 mmol) at room

temperature, and the mixture was stirred at the same temperature for 2h. The reaction was quenched by addition of H_2O (50 mL), and the mixture was extracted by ethyl acetate (3 x 50 mL). The combined organic extracts were washed with saturated $NaHCO_3$, and dried with $MgSO_4$, the solvent was removed under vacuum, and the residue was purified by a flash chromatography (hexane/ethyl acetate) on silica gel to give 2.35 g of 5-(5-(4-chlorophenyl)furan-3-yl)pentyl acetate as the pale yellow oil in the quantitative yield.

To a solution of 5-(5-(4-chlorophenyl)furan-3-yl)pentyl acetate (1.53 g, 5.0 mmol) in *N*,*N*-dimethyl formamide (25 mL) was added a solution of *N*,*N*-dimethyl formamide (10 mL) and phosphorus oxychloride (0.92 g, 6.0 mmol) at 0°C under nitrogen, and the resultant mixture was first stirred at to room temperature for 30 min, and then at 60°C for 2 h. The reaction was worked by addition of a saturated solution of Na_2CO_3 at 0 °C to neutralize topH 6, and the mixture was extracted with ethyl acetate twice. The combined organic extracts was washed with saturated $NaHCO_3$, and then dried with $MgSO_4$,.The solvent was removed under vacuum, and the residue was purified by a flash chromatography (hexane/ethyl acetate) on silica gel to give 5-(5-(4-chlorophenyl)- 2-formylfuran-3-yl)pentyl acetate **9** (1.34 g, 80% in two steps) as pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.76 (s, 1H), 7.72 (d, J = 8.7 Hz, 2H), 7.41 (d, J = 11 Hz, 2H), 6.70 (s, 1H), 4.06 (t, J = 6.0 Hz, 2H), 2.84 (t, J = 6.0 Hz, 2H), 2.03 (s, 3H), 1.72-1.63 (m, 4H), 1.49-1.41 (m, 2H); HRMS (ESI) calcd for $C_{18}H_{20}ClO_4$ $[M + H]^+$ 335.1050, found 335.1043.

Synthesis of 5-(4-chlorophenyl)-3-(5-hydroxypentyl)furan-2-carbaldehyde **10**:

To the solution of 5-(5-(4-chlorophenyl)-2-formylfuran-3-yl)pentyl acetate **9** (1.0 g, 3.0 mmol) in MeOH was added K_2CO_3 (2.07 g, 15.0 mmol), the suspension was stirred at room temperature until **9** was fully consumed (1 h). The reaction was worked up by addition of H_2O, the resultant mixture was extracted with EA. The combined organic phases were concentrated; the residue was purified by a flash chromatography (hexane/ethyl acetate) on silica gel to give 5-(4-chlorophenyl)- 3-(5-hydroxypentyl)furan-2-carbaldehyde **10** (0.88 g, ~100%) as pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.73 (s, 1H), 7.72 (d, J = 13 Hz, 2H), 7.37 (d, J = 13 Hz, 2H),6.69 (s, 1H), 3.64 (t, J = 6.3 Hz, 2H), 2.81 (t, J =7.2 Hz, 2H), 1.89 (broad, 1H), 1.71-1.56 (m, 4H), 1.49-1.41 (m, 2H); HRMS (ESI) calcd for $C_{16}H_{18}ClO_3$ $[M + H]^+$ 293.0944, found 293.0937.

Synthesis of *(Z)*-(+/-)-*exo*-3-(bicyclo[2.2.1]heptan-2-yl)-5-((5-(4-chlorophenyl)-3-(5-hydroxy-pentyl)- furan-2-yl)methylene)-2-thioxothiazolidin-4-one **11**:

To a solution of (+/-)-*exo*-3-(bicyclo[2.2.1]heptan-2-yl)-2-thioxothiazolidin-4-one **3** (0.14 g, 0.6 mmol) and 5-(4-chlorophenyl)- 3-(5-hydroxypentyl)furan-2-carbaldehyde **10** (0.15 g, 0.5 mmol) in EtOH (5 mL) was added a catalytic amount of anhydrous piperidine (two drops) at room temperature, and the mixture was stirred for 12 h. The reaction was worked up by addition of ethyl acetate (50 mL), and the combined organic extracts were washed with water (3 x 10 mL), and then dried over anhydrous Na_2SO_4. The solvent was removed under vacuum, and the residue was purified by a flash chromatography (ethyl acetate/hexane) to afford *(Z)*-(+/-)-*exo*-3-(bicyclo[2.2.1]heptan-2-yl)-5-((5-(4-chlorophenyl)-3-(5-hydroxylpentyl)furan -2-yl)-mthylene)-2-thioxothiazolidin-4-one **11** (0.19 g, 75%) as red solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (d, J = 8.7 Hz, 2H), 7.43 (d, J = 8.7 Hz, 2H), 7.38 (s, 1H), 6.72 (s, 1H), 4.97 (td, J = 8.4, 6.0 Hz, 1H), 3.66 (t, J = 6.3 Hz, 2H), 2.62 (t, J = 7.2 Hz, 2H), 2.55 (s, 1H), 2.46 (s, 1H), 2.40-2.23 (m, 2H), 1.75 (t, J = 7.3, 2.4 Hz, 1H), 1.76-1.63 (m, 3H),

1.60-1.40 (m, 4H); HRMS (ESI) calcd for $C_{26}H_{29}ClNO_3S_2$ $[M + H]^+$ 502.1277, found 502.1265.

Synthesis of *(Z)*-(+/-)-*exo*-3-(bicyclo[2.2.1]heptan-2-yl)-5-((5-(4-chlorophenyl)-3-(5-iodo-pentyl)furan-2-yl)-methylene)-2-thioxothiazolidin-4-one **12**:

To a solution of *(Z)*-(+/-)-*exo*-3-(bicyclo[2.2.1]heptan-2-yl)-5-((5-(4-chlorophenyl)-3-(5-hydroxy-pentyl)furan-2-yl)methylene)-2-thioxothiazolidin-4-one **11** (0.15 g, 0.30 mmol), PPh_3 (0.12 g, 0.46 mmol) and imidazole (0.04 g, 0.60 mmol) in THF (60 mL) was added I_2 (0.10 g, 0.40 mmol), the mixture was stirred at room temperature for 2h. The solvent were removed, and the residue was extracted with EA, and the combined organic extracts were washed with a saturated solution of $Na_2S_2O_3$ and then dried $MgSO_4$. The solvent was removed under vacuum, and the residue was purified by a flash chromatography (ethyl acetate/hexane) on silica gel to give *(Z)*-(+/-)-*exo*-3-(bicyclo[2.2.1]heptan-2-yl)-5-((5-(4-chlorophenyl)-3-(5-iodopentyl)furan-2-yl)-methylene)-2-thioxothiazolidin-4-one **12** (0.13 g, 70%) as yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 (d, J = 11 Hz, 1H), 7.43 (d, J = 8.7 Hz, 1H), 7.36 (s, 1H), 6.73 (s, 1H), 6.71 (d, J = 3.6 Hz, 1H), 4.97 (td, J = 8.7, 6.0 Hz, 1H), 2.86 (t, J = 7.2 Hz, 2H), 2.67 (t, J = 7.2 Hz, 2H), 2.46 (s, 1H), 2.40-2.23 (m, 2H), 1.82 (dt, J = 7.3, 2.4 Hz, 1H), 1.76-1.63 (m, 3H), 1.60-1.40 (m, 4H); HRMS (ESI) calcd for $C_{26}H_{28}ClINO_2S_2$ $[M + H]^+$ 612.0295, found 612.0285.

Synthesis of *(Z)*-(+/-)-*exo*-*tert*-butyl 4-(5-(2-((3-(bicyclo[2.2.1]heptan-2-yl)-4-oxo-2-thioxo-thiazolidin-5-ylidene)methyl)-5-(4-chlorophenyl)furan-3-yl)pentyl)piperazine-1-carboxylate **13**:

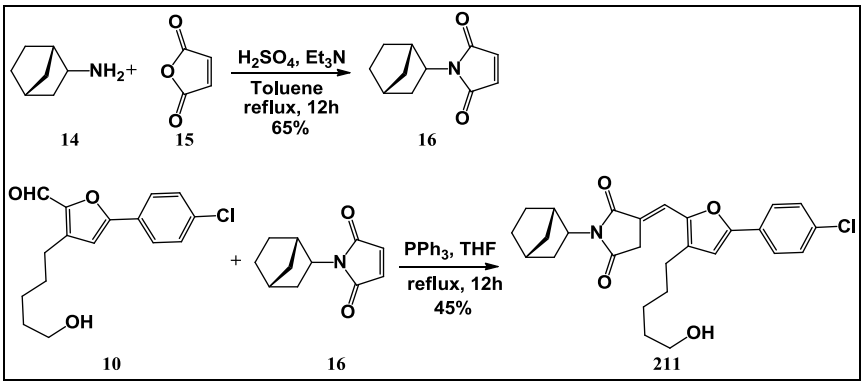
To a solution of *(Z)*-(+/-)-*exo*-3-(bicyclo[2.2.1]heptan-2-yl)-5-((5-(4-chlorophenyl)-3-(5 -iodopentyl)furan-2-yl)methylene)-2-thioxothiazolidin-4-one **12** (0.12 g, 0.20 mmol) in dry DCM (10 mL) was added *tert*-butyl piperazine-1-carboxylate (0.08 g, 0.43 mmol), and the mixture was stirred at room temperature for 12 h. The solvent was removed, and the residue was purified by a flash chromatography (ethyl acetate/hexane) on silica gel to give *(Z)*-(+/-)-*exo*-*tert*-butyl 4-(5-(2-((3-(bicyclo[2.2.1]heptan-2-yl)-4-oxo-2-thioxothiazolidin-5-ylidene)-methyl)-5-(4-chlorophenyl)furan-3-yl)pentyl)piperazine-1-carboxylate **13** (0.12 g, 90%) as red solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 (d, J = 8.7 Hz, 2H), 7.45 (d, J = 8.4 Hz, 2H), 7.39 (s, 1H), 6.74 (s, 1H), 4.90 (dd, J = 8.7, 6.3 Hz, 1H), 3.45 (broad, 4H), 2.64-2.57 (m, 3H), 2.48-2.30 (m, 10H), 1.90-1.53 (m, 7H), 1.50 (s, 9H), 1.48-1.20 (m, 6H); HRMS (ESI) calcd for $C_{35}H_{45}ClN_3O_4S_2$ $[M + H]^+$ 670.2540, found 670.2542.

Synthesis of *(Z)*-(+/-)-*exo*-3-(bicyclo[2.2.1]heptan-2-yl)-5-((5-(4-chlorophenyl)-3-(5-(piperazin-1-yl)-pentyl)furan-2-yl)methylene)-2-thioxothiazolidin-4-one dihydrochloride **136**:

(Z)-(+/-)-*exo*-*tert*-butyl 4-(5-(2-((3-(bicyclo[2.2.1]heptan-2-yl)-4-oxo-2-thioxothiazolidin -5-ylidene)- methyl)-5-(4-chlorophenyl)furan-3-yl)pentyl)piperazine-1-carboxylate **13** (0.12 g, 0.18 mmol) was mixed with a saturated solution of HCl (gas) in methanol (20 mL) at 0 ^{o}C, and the resultant mixture was stirred at room temperature for 2 h. The reaction was worked up by removal of the organic solvent under vacuum, and the residue was purified by a recrystallization from diethyl ether to give *(Z)*-(+/-)-*exo*-3-(bicyclo[2.2.1]heptan-2-yl)-5-((5-(4-chlorophenyl)-3-(5-(piperazin-1-yl)-pentyl)furan-2-yl)methylene)-2-thioxothiazolidin-4-one dihydrochloride **136** (0.12 g, ~100%) as reddish brown solid. ^{1}H NMR (300 MHz,

DMSO-d_6) δ 11.8 (board, 1H), 9.72 (board, 2H), 7.81 (d, J = 9.0 Hz, 2H), 7.65 (d, J = 6.0 Hz, 2H), 7.46 (s, 1H), 7.37 (s, 1H), 4.85 (t, J = 6.0 Hz, 1H), 3.56-3.53 (m, 2H), 3.48-3.39 (m, 4H), 3.26-3.19 (m, 2H), 3.35-3.12 (m, 4H), 2.66 (t, J = 7.2 Hz, 2H), 2.37 (s, 1H), 2.28-2.19 (m, 2H), 1.74-1.63 (m, 4H), 1.54-1.53 (m, 2H), 1.40-1.36 (m, 2H), 1.25-1.20 (m, 3H); ^{13}C NMR (75.5 MHz, DMSO-d_6) δ 196.1, 167.1, 156.3, 146.2, 137.9, 133.9, 129.6, 127.5, 126.2, 117.4, 115.5, 111.9, 62.4, 55.6, 47.9, 37.8, 36.3, 35.3, 29.3, 28.0, 26.0, 24.6, 23.0; HRMS (ESI) calcd for $C_{30}H_{39}Cl_3N_3O_2S_2$ [M – 2HCl + H]$^+$ 570.2016, found 570.1943.

- General procedure for the synthesis of (*E*)- *endo/exo*-1-(bicyclo[2.2.1]heptan-2-yl)-3-((5-(4-chlorophenyl)-3-(5-hydroxy-pentyl)- furan-2-yl)methylene)pyrrolidine-2,5-dione **211**:



Synthetic route of inhibitor **211**

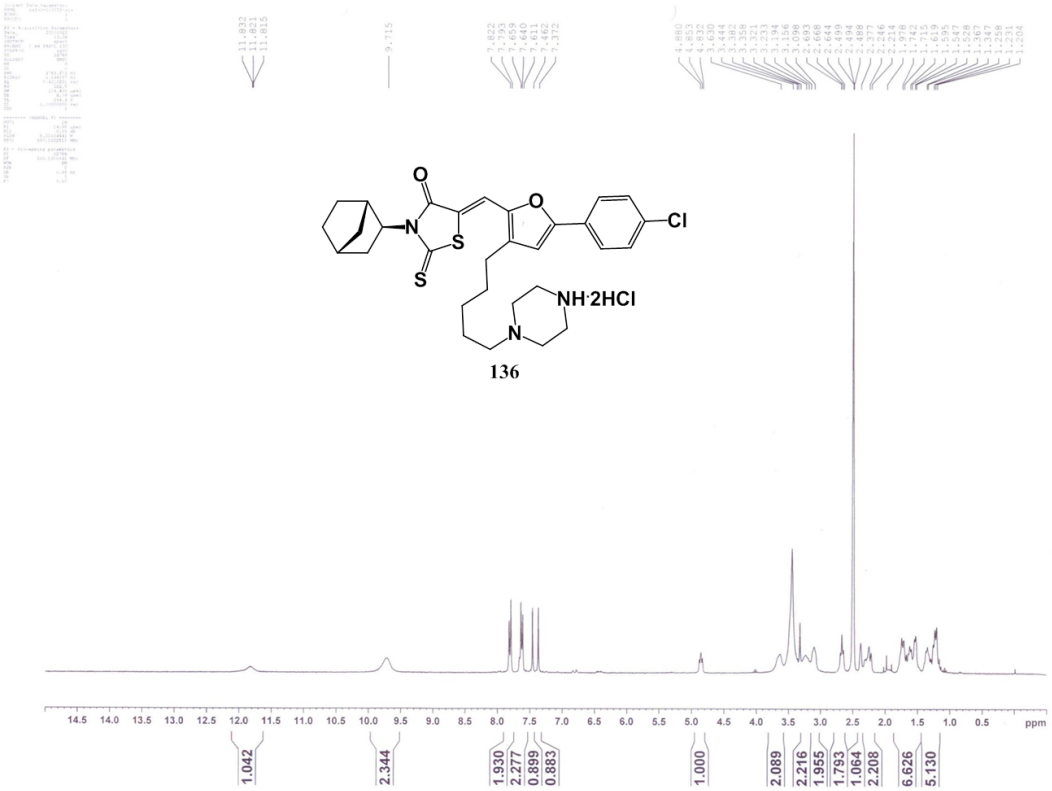
Synthesis of *endo/exo*-1-(bicyclo[2.2.1]heptan-2-yl)-1H-pyrrole-2,5-dione **16**:
To a solution of 1-bicyclo[2.2.1]heptan-2-amine **14** (3.36 g, 30.0 mmol, mixture of *endo* and *exo*, purchased from J&K Chemicals Co.) and furan-2,5-dione **15** (1.98 g, 20.0 mmol) in toluene (150 mL) was added H_2SO_4 (5.0 mL) and Et_3N (5.0 mL) and the mixture was stirred under refluxing conditions for 12h. After removal of the solvents, the residue was resolved in ethyl acetate (150 mL), and the organic phase was washed sequentially with H_2O, $NaHCO_3$, and brine (20 mL), and finally dried over anhydrous Na_2SO_4. After removal of the solvent under vacuum, the crude product was purified by a flash column chromatography on silica gel (ethyl acetate/hexane) to afford *endo/exo*-1-(bicyclo[2.2.1]heptan-2-yl)-1H-pyrrole-2,5-dione **16** (2.51 g, *endo*:*exo* = 5:2, 65%) as whit solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.76 (s, 1H), 4.31-4.10 (m, 0.75H), 4.00-3.85 (m, 0.25H), 2.52-2.05 (m, 4H), 1.62-1.50 (m, 3H), 1.40-1.25 (m, 3H); HRMS (ESI) calcd for $C_{11}H_{13}NO_2Na$ [M + Na]$^+$ 214.0844, found 214.0838.

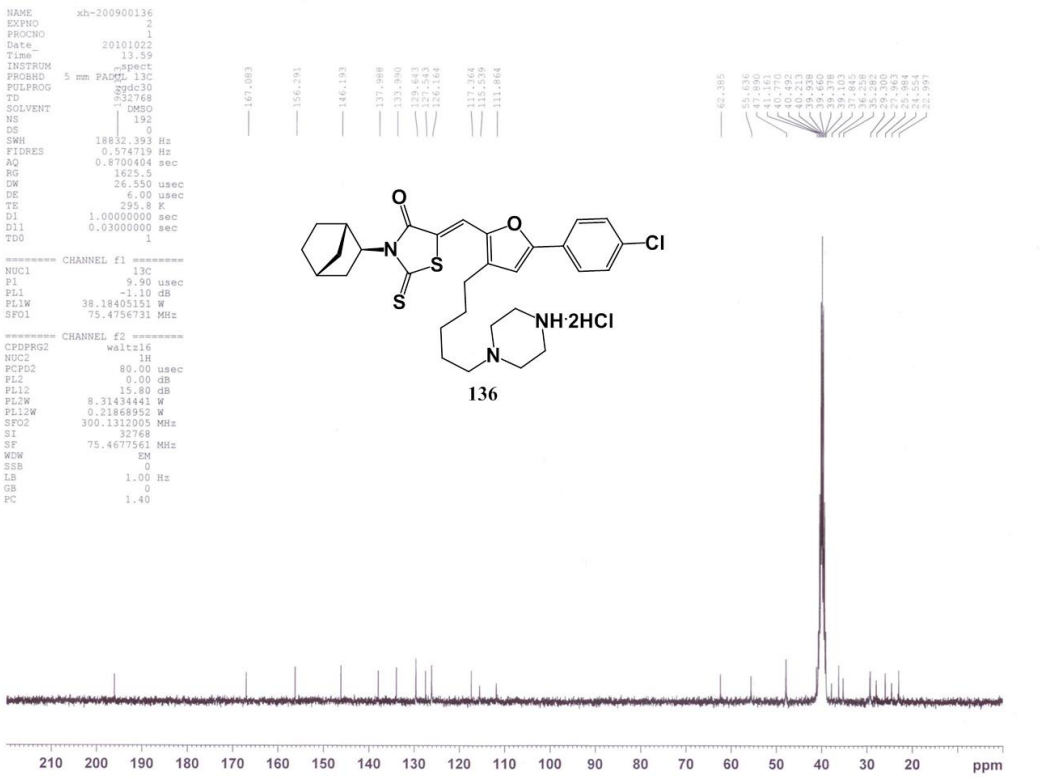
Synthesis of (*E*)-*endo/exo*-1-(bicyclo[2.2.1]heptan-2-yl)-3-((5-(4-chlorophenyl)-3-(5-hydroxylpentyl)-furan-2-yl)methylene)pyrrolidine-2,5-dione **211**:

To a solution of 5-(4-chlorophenyl)-3-(5-hydroxypentyl)furan-2-carb-aldehyde **10** (1.46 g, 5.0 mmol) and *endo/exo*-1-(bicyclo[2.2.1]heptan-2-yl)-1H-pyrrole-2,5-dione **16** (0.96 g, *endo*:*exo* = 5:2, 5.0 mmol) in dry THF (50 mL) was added PPh_3 (1.31 g, 5.0 mmol), and the mixture was stirred under refluxing conditions for 12h. The reaction was worked up by removal of the solvents, and the residue was resolved in ethyl acetate (150 mL), then washed with brine (20 mL), and finally dried over anhydrous Na_2SO_4. The solvent was removed under vacuum, and the residue was purified by a flash chromatography (ethyl acetate/hexane)

on silica gel to give (*E*)-*endo/exo*-1-(bicyclo[2.2.1]-heptan-2-yl)-3-((5-(4-chlorophenyl) -3-(5-hydroxypentyl)furan-2-yl)- methylene)pyrrolidine-2,5-dione **211** (1.05 g, *end*:*exo* = 5:2, 45%) as yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 8.6 Hz, 2H), 7.41 (d, J = 8.4 Hz, 2H), 7.37-7.34 (m, 1H), 6.70 (s, 1H), 4.50-4.39 (m, 0.75H), 4.15-4.05 (m, 0.25H), 3.73 (d, J = 2.0 Hz, 1H), 3.70-3.65 (m, 2H), 2.62 (td, J = 7.2, 3.2 Hz, 2H), 2.54 (s, 1H), 2.39 (s, 1.4H), 2.30-2.20 (m, 0.75H), 1.90-1.75 (m, 3H), 1.54-1.20 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.96, 156.73, 146.46, 137.11, 134.88, 129.32, 127.37, 125.80, 118.13, 115.15, 110.00, 62.63, 41.40, 37.93, 36.48, 35.49, 32.33, 30.04, 29.46, 27.90, 25.35, 25.15; HRMS (ESI) calcd for $C_{27}H_{30}ClNO_4Na$ $[M + Na]^+$ 490.1761, found 490.1754.

Spectrum data of compounds 136 and 211:

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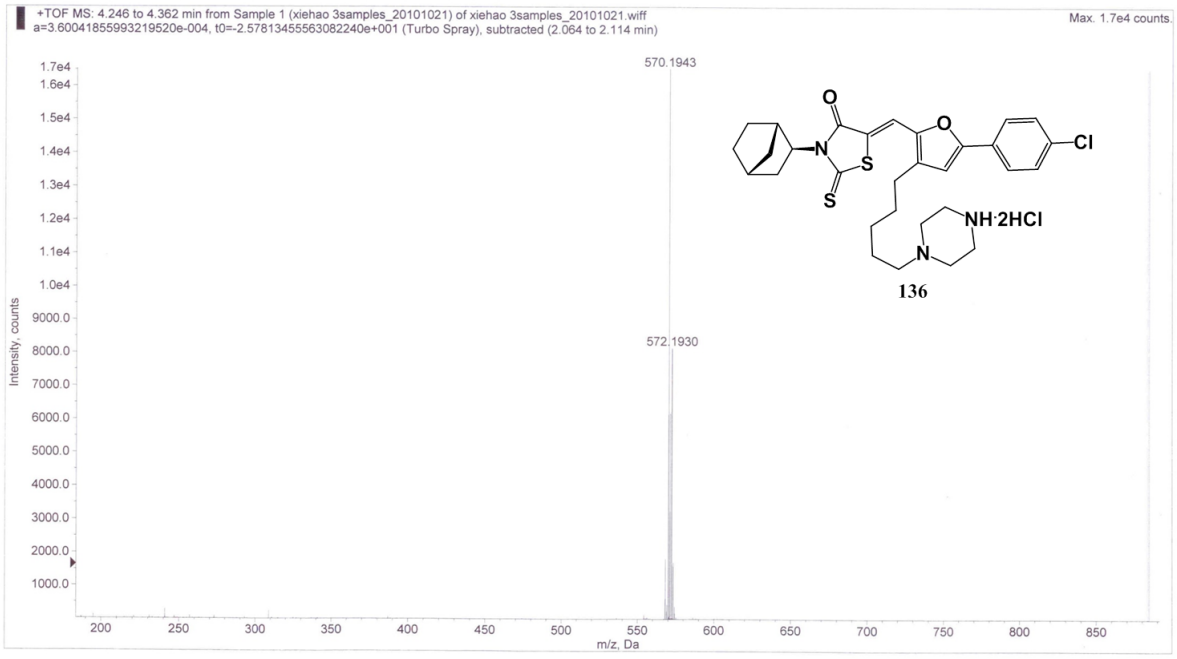
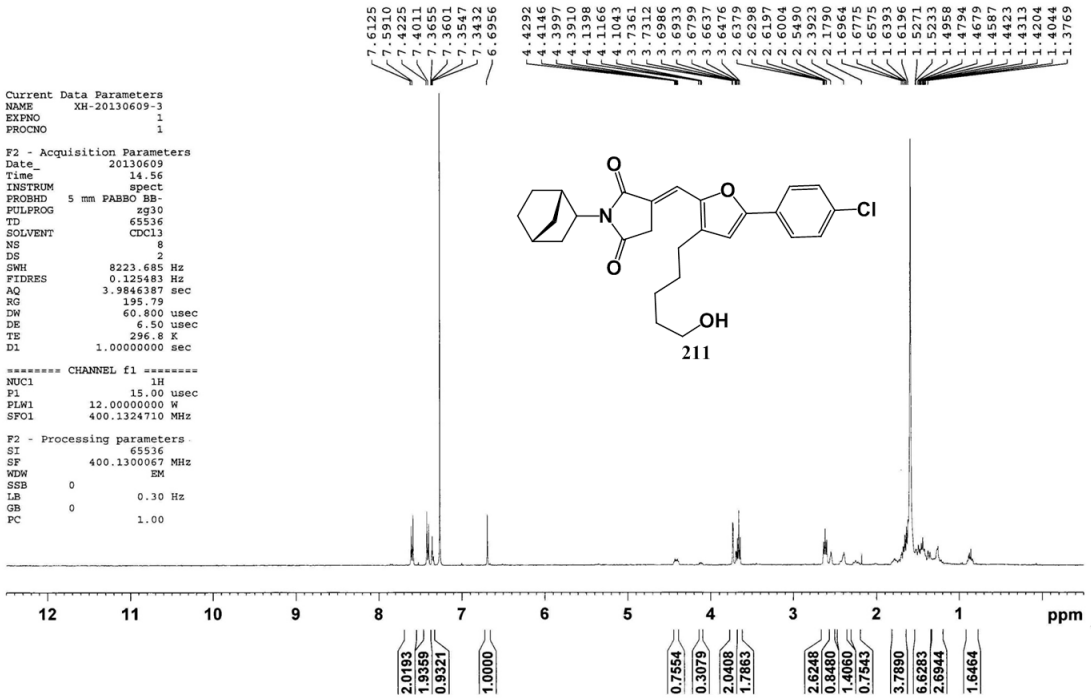
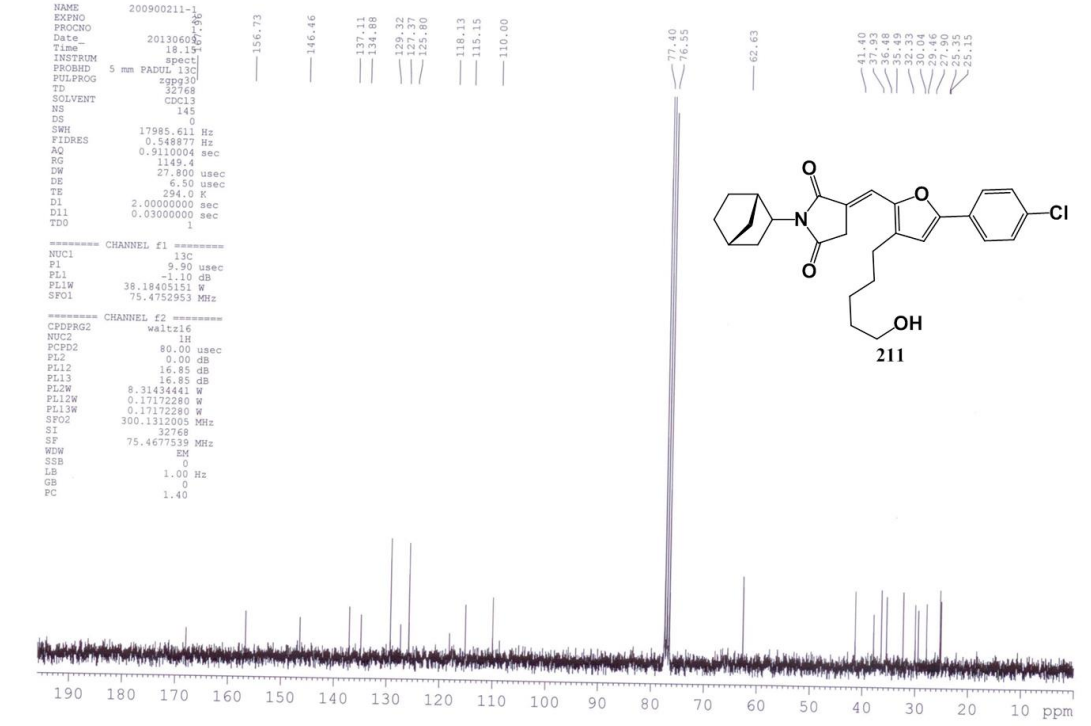
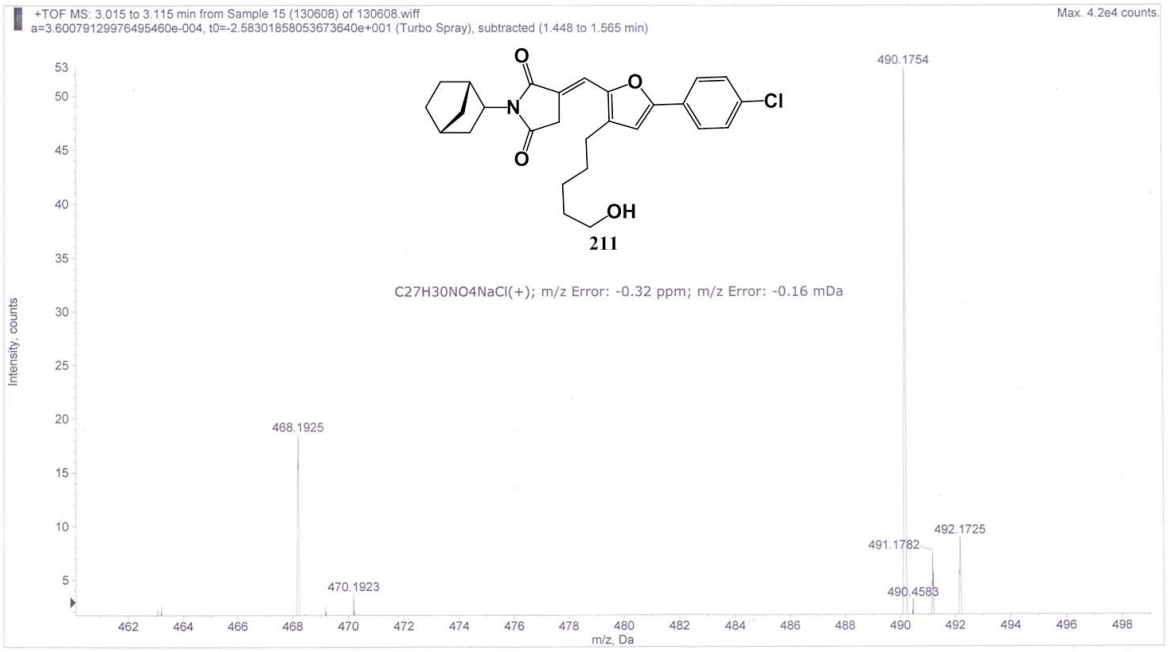
======== CHANNEL f1 ========
NUC1 13C
P1 9.90 usec
PL1 -1.10 dB
PL1W 38.18405151 W
SFO1 75.4756731 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 0.00 dB
PL12 15.80 dB
PL2W 8.31434441 W
PL12W 0.21868952 W
SFO2 300.1312005 MHz
SI 32768
SF 75.4677561 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
167.083
156.291
146.193
137.988
133.940
129.643
127.543
126.164
117.364
115.539
111.864
62.385
55.696
47.961
41.161
40.770
40.492
40.213
39.938
39.660
39.378
39.103
38.841
36.258
35.282
29.960
29.746
25.984
24.554
22.997
O
N
S
O
Cl
S
NH·2HCl
N
136
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

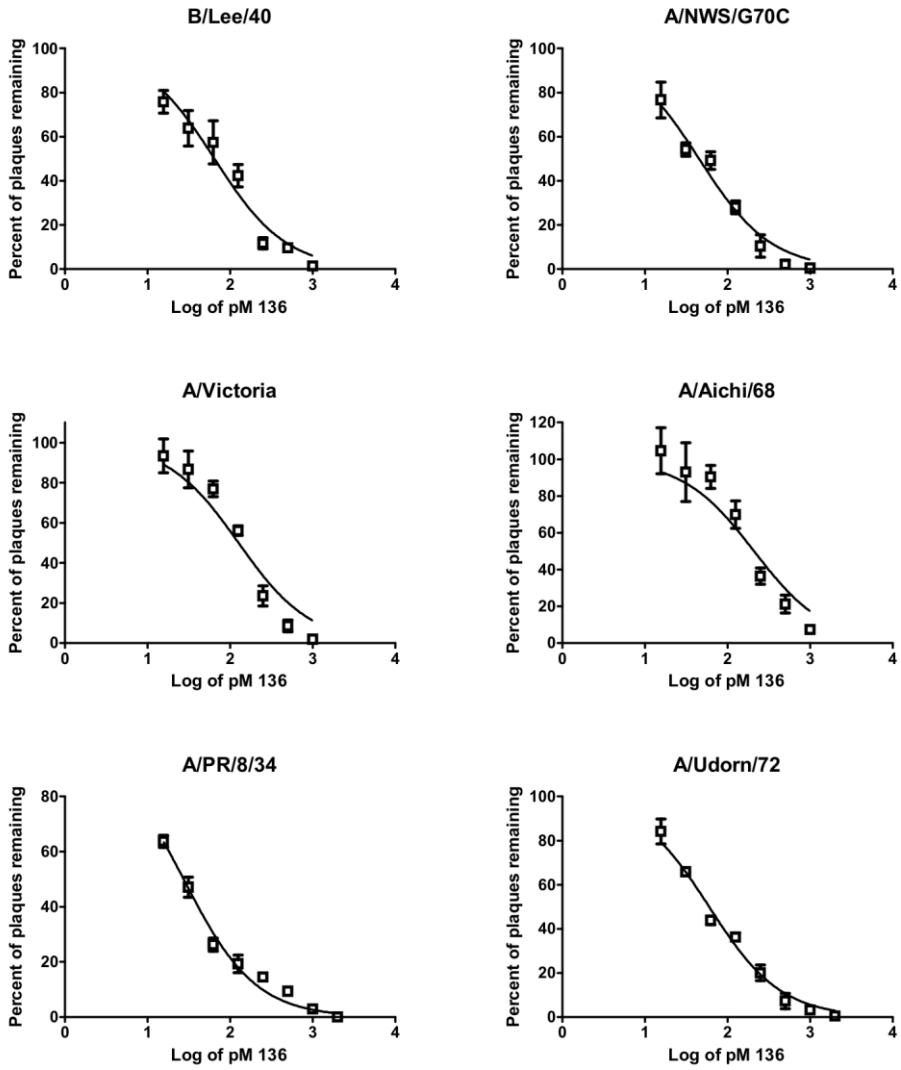

+TOF MS: 4.246 to 4.362 min from Sample 1 (xiehao 3samples_20101021) of xiehao 3samples_20101021.wiff
a=3.60041855993219520e-004, t0=-2.57813455563082240e+001 (Turbo Spray), subtracted (2.064 to 2.114 min)
Max. 1.7e4 counts.
570.1943
572.1930
O
N
S
O
Cl
S
NH·2HCl
N
136
Intensity, counts
1.7e4
1.6e4
1.5e4
1.4e4
1.3e4
1.2e4
1.1e4
1.0e4
9000.0
8000.0
7000.0
6000.0
5000.0
4000.0
3000.0
2000.0
1000.0
200 250 300 350 400 450 500 550 600 650 700 750 800 850
m/z, Da


7.6125
7.5910
7.4225
7.4011
7.3655
7.3601
7.3547
7.3432
6.6956
4.4292
4.4146
4.3997
4.3910
4.1398
4.1166
4.1043
3.7361
3.7312
3.6986
3.6933
3.6799
3.6637
3.6476
2.6379
2.6298
2.6197
2.6004
2.5490
2.3923
2.1790
1.6964
1.6775
1.6575
1.6393
1.6196
1.5271
1.5233
1.4958
1.4794
1.4679
1.4587
1.4423
1.4313
1.4204
1.4044
1.3769
Current Data Parameters
NAME XH-20130609-3
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130609
Time 14.56
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 8
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 195.79
DW 60.800 usec
DE 6.50 usec
TE 296.8 K
D1 1.00000000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 15.00 usec
PLW1 12.00000000 W
SFO1 400.1324710 MHz
F2 - Processing parameters
SI 65536
SF 400.1300067 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
O
N
O
O
Cl
OH
211
12
11
10
9
8
7
6
5
4
3
2
1
ppm
2.0193
1.9359
0.9321
1.0000
0.7554
0.3079
2.0408
1.7863
2.6248
0.8480
1.4060
0.7543
3.7890
6.6283
2.6944
1.6464

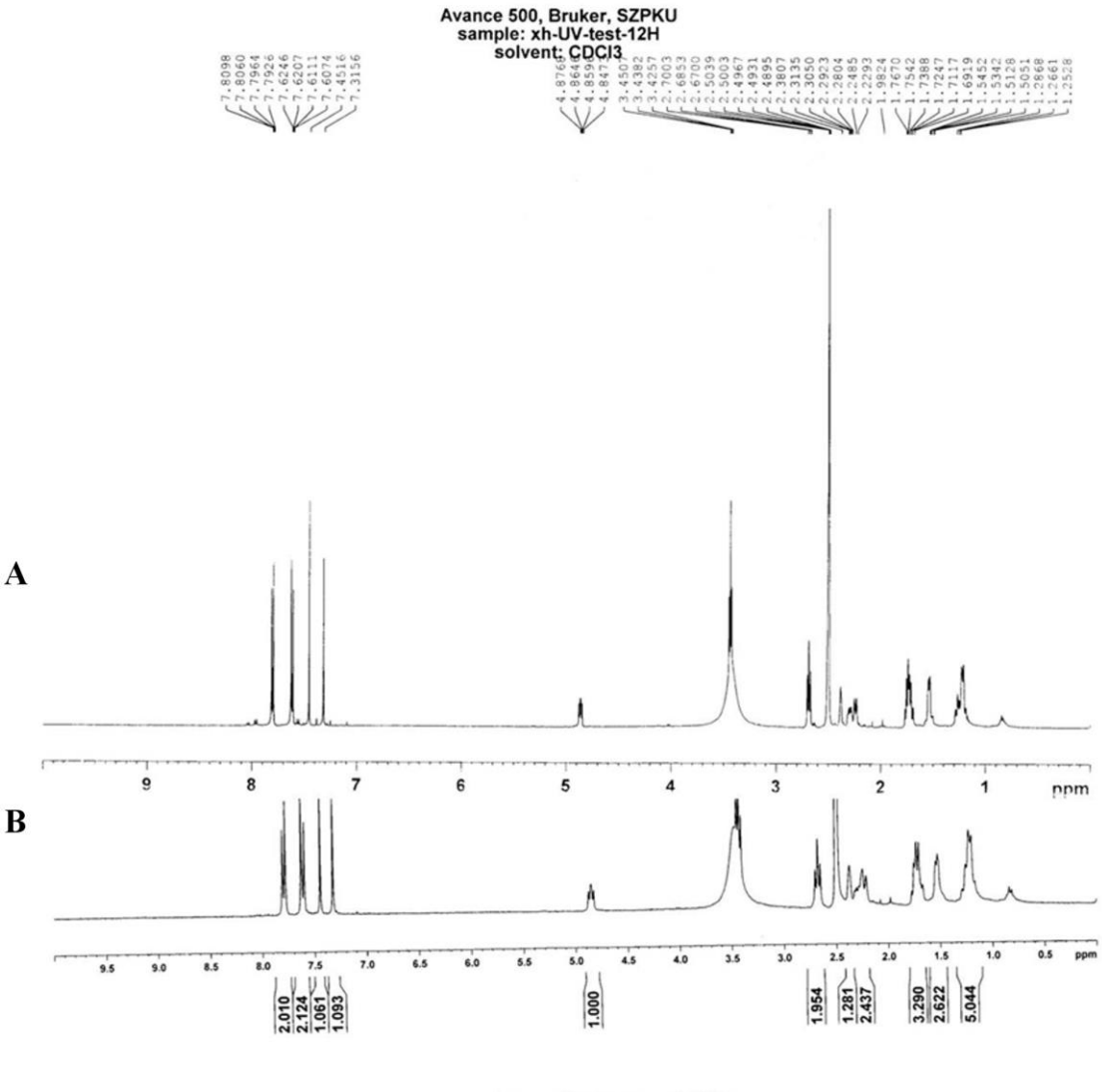

NAME 200900211-1
EXPNO
PROCNO
Date_ 20130609
Time 18.19
INSTRUM spect
PROBHD 5 mm PADUL 13C
PULPROG zgpg30
TD 32768
SOLVENT CDCl3
NS 145
DS 0
SWH 17985.611 Hz
FIDRES 0.548877 Hz
AQ 0.9110004 sec
RG 1149.4
DW 27.800 usec
DE 6.50 usec
TE 294.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.90 usec
PL1 -1.10 dB
PL1W 38.18405151 W
SFO1 75.4752953 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 0.00 dB
PL12 16.85 dB
PL13 16.85 dB
PL2W 8.31434441 W
PL12W 0.17172280 W
PL13W 0.17172280 W
SFO2 300.1312005 MHz
SI 32768
SF 75.4677539 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
167.96
156.73
146.46
137.11
134.88
129.32
127.37
125.80
118.13
115.15
110.00
77.40
76.55
62.63
41.40
37.93
36.48
35.49
32.33
30.04
29.46
27.90
25.35
25.15
O
N
O
O
Cl
OH
211
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


+TOF MS: 3.015 to 3.115 min from Sample 15 (130608) of 130608.wiff
a=3.60079129976495460e-004, t0=-2.58301858053673640e+001 (Turbo Spray), subtracted (1.448 to 1.565 min)
Max. 4.2e4 counts.
O
N
O
O
Cl
OH
211
C27H30NO4NaCl(+); m/z Error: -0.32 ppm; m/z Error: -0.16 mDa
Intensity, counts
m/z, Da
490.1754
468.1925
492.1725
491.1782
470.1923
490.4583

S1 Fig. The plaque reduction assays of 136 against many different influenza virus strains



S2 Fig. 136 NMR profiles.



S1 Table. 136 does not alter the pH of virus preparations.

	Trial 1	Trial 2	Trial 3
Control	7.96	8.01	8.00
DMSO	7.97	7.96	8.02
50 pM 136	7.95	7.96	8.03
5 μM 136	8.00	8.01	7.97